*Note: This is a two-article spread with a shared commentary. Please scroll down for the second article.*

# Whole-blood antibody tests were not highly sensitive for detecting *Helicobacter pylori* infection

Chey WD, Murthy U, Shaw S, et al. **A comparison of three fingerstick, whole blood antibody tests for *Helicobacter pylori* infection: a United States, multicenter trial.** Am J Gastroenterol. 1999 Jun;94:1512-6.

### Question

How accurate are whole-blood antibody tests for diagnosing *Helicobacter pylori* infection?

### Design

Blinded comparison of 3 whole-blood antibody tests with tests based on endoscopic biopsy.

### Setting

3 medical centers in the United States (Ann Arbor, Michigan; Syracuse, New York; and Los Angeles, California).

### Patients

131 patients who were 19 to 87 years of age (mean age 54 y, 59% men) and were referred for upper endoscopy. Exclusion criteria were treatment for *H. pylori* infection in the previous year or use of antibiotics or bismuth-containing compounds in the previous month or a proton-pump inhibitor in the previous 7 days.

### Description of tests and diagnostic standards

The 3 whole-blood antibody tests were FlexPack HP (Abbott Diagnostics, Abbott Park, IL, USA), QuickVue (Quidel Corporation, San Diego, CA, USA), and AccuMeter (formerly HpChek; ChemTrak, Sunnyvale, CA, USA). Antibody testing was done by using whole blood obtained with 2 or 3 fingersticks. The 3 diagnostic standards were histologic evidence of *H. pylori* infection in biopsies taken from the body and the antrum of the stomach, positive results with both histologic and rapid urease testing (RUT) (excluding 12 patients with discordant histologic and RUT results), and a positive result on either histologic testing or RUT.

### Main outcome measures

Sensitivity and specificity for detecting *H. pylori* infection.

### Main results

Sensitivities, specificities, and likelihood ratios for tests are shown in the Table.

### Conclusion

Whole-blood antibody tests were not highly sensitive for detecting *Helicobacter pylori* infection.

*Source of funding: Not stated.*

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**Test characteristics for detecting *Helicobacter pylori* infection***

| Diagnostic standards | Tests | Sensitivity (95% CI) | Specificity (CI) | +LR | –LR |
|---|---|---|---|---|---|
| Histologic testing | FlexPack | 76% (62 to 87) | 79% (69 to 87) | 3.6 | 0.3 |
| | QuickVue | 78% (64 to 88) | 90% (81 to 96) | 7.9 | 0.2 |
| | AccuMeter | 84% (71 to 93) | 90% (81 to 96) | 8.5 | 0.2 |
| | RUT | 88% (76 to 95) | 93% (85 to 97) | 11.9 | 0.1 |
| Histologic testing and RUT | FlexPack | 77% (62 to 89) | 80% (69 to 88) | 3.9 | 0.3 |
| | QuickVue | 82% (67 to 92) | 91% (82 to 96) | 8.8 | 0.2 |
| | AccuMeter | 89% (75 to 96) | 92% (83 to 97) | 11.1 | 0.1 |
| Histologic testing or RUT | FlexPack | 73% (60 to 84) | 81% (71 to 89) | 3.9 | 0.3 |
| | QuickVue | 71% (58 to 83) | 91% (82 to 96) | 7.7 | 0.3 |
| | AccuMeter | 79% (66 to 88) | 92% (83 to 97) | 9.8 | 0.2 |

*RUT = rapid urease testing. LRs defined in Glossary and calculated from data in article.

## Commentary

Consensus statements in North America and Europe have supported a strategy of "test and eradicate *H. pylori*" for the management of dyspepsia in the office setting. This strategy benefits patients by breaking the cycle of recurrence of duodenal ulcer disease and decreasing the risk for developing future gastric cancer (1). The cost benefit of this strategy lies in avoiding endoscopy; therefore, accurate and reliable nonendoscopic tests for *H. pylori* are needed (2).

These studies by Chey and colleagues examine the performance of 2 such tests: whole-blood tests done at the point of care to identify antibodies to *H. pylori* and a $^{13}$C-urea blood test. The latter is a new technique based on the $^{13}$C-urea breath test in which $^{13}CO_2$ is released from ingested $^{13}$C-urea if *H. pylori*, with its urease enzyme, is present in the stomach. Rather than requiring pre- and post-breath samples, a single blood test can be done 30 minutes after ingestion to identify $^{13}$C-bicarbonate by mass spectrometry.

Important differences exist between the antibody and urease-based technologies. The whole-blood tests give an immediate result and can be done in 5 to 10 minutes. The $^{13}$C-urea blood test requires more staff input, a 30-minute delay before sample collection, and fasting for patients. The sample has to be sent to a central laboratory for analysis, and the result and subsequent therapeutic decision are delayed.

The essential question underlying these 2 studies is whether the additional accuracy of the urea blood test is worth the additional cost. This question has 2 parts. First, what is the difference in performance of the 2 tests in the office setting? Second, what patient-related benefits are obtained by that difference? As Chey and colleagues state, no gold standard exists for identifying *H. pylori,* and most evaluations use a proxy of several reference tests combined. Chey and colleagues' approach is a base-case evaluation that uses histologic testing alone with a biopsy-based urease test as an additional reference standard for calculating test performance under the worst and best conditions.

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# The $^{13}$C-urea blood test is accurate for detecting *Helicobacter pylori* infection

Chey WD, Murthy U, Toskes P, Carpenter S, Laine L. **The $^{13}$C-urea blood test accurately detects active *Helicobacter pylori* infection: a United States, multicenter trial.** Am J Gastroenterol. 1999 Jun;94:1522-4.

### QUESTION

How accurate is the $^{13}$C-urea blood test for detecting *Helicobacter pylori* infection?

### DESIGN

Blinded comparison of the $^{13}$C-urea blood test with tests based on endoscopic biopsy.

### SETTING

5 centers in the United States (Ann Arbor, Michigan; Syracuse, New York; Gainesville, Florida; Savannah, Georgia; and Los Angeles, California).

### PATIENTS

121 patients (mean age 49 y, 51% men) who were referred for endoscopy. Exclusion criteria included therapy for *H. pylori* infection in the previous year or use of antibiotics or bismuth in the previous month or proton-pump inhibitors in the previous 7 days.

### DESCRIPTION OF TESTS AND DIAGNOSTIC STANDARDS

Patients received $^{13}$C-urea, 125 mg dissolved in 75 mL of water. 30 minutes later, a 3-mL blood sample was obtained by venipuncture and analyzed by gas isotope ratio mass spectrometry. The 3 diagnostic standards were histologic evidence of *H. pylori* infection in biopsies obtained from the body and antrum of the stomach, a positive result for both histologic and rapid urease testing (RUT) (patients with discordant histologic and RUT results were considered uninfected), and a positive result for either histologic testing or RUT.

### MAIN OUTCOME MEASURES

Sensitivity and specificity for detecting *H. pylori* infection.

### MAIN RESULTS

Sensitivities, specificities, and likelihood ratios are shown in the Table. Results for the $^{13}$C-urea blood test did not differ from those for RUT ($P > 0.2$).

### CONCLUSION

The $^{13}$C-urea blood test was similar to rapid urease testing and had high sensitivity and specificity for detecting *Helicobacter pylori* infection.

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**Test characteristics for detecting *Helicobacter pylori* infection***

| Diagnostic standards | Tests | Sensitivity (95% CI) | Specificity (CI) | +LR | –LR |
|---|---|---|---|---|---|
| Histologic testing | $^{13}$C-UBT<br>RUT | 89% (85 to 93)<br>87% (75 to 95)† | 96% (94 to 98)<br>96% (87 to 99)† | 19.9<br>19.4† | 0.1<br>0.1† |
| Histologic testing and RUT | $^{13}$C-UBT | 94% (87 to 100)‡ | 91% (85 to 97)‡ | 10.4 | 0.1 |
| Histologic testing or RUT | $^{13}$C-UBT | 88% (80 to 96)‡ | 98% (95 to 100)‡ | 44.0 | 0.1 |

*$^{13}$C-UBT = $^{13}$C-urea blood test; RUT = rapid urease testing. LRs defined in Glossary and calculated from data in article.
†Calculated from data supplied by author.
‡CIs provided by author.

## COMMENTARY *(continued from page 34)*

The combination of reference standard error, spectrum bias, and a greater potential for operator error means that caution should be used when extrapolating these results to the office setting (3).

Unfortunately, although the absolute values of the performance of the $^{13}$C-urea blood test are greater than the whole-blood antibody tests, the confidence intervals overlap, which means that we cannot be certain that the difference is robust. In any case, clinical differences between the 2 types of tests will be small because, at most, only 20% of patients will benefit from the "test and eradicate" strategy (4), and the absolute difference in sensitivity of the tests is only 5% to 10% (1). Only 2 patients in 100 might be missed with the antibody test. An evaluation of the tests in the office setting with larger samples and a health economic analysis are needed before an informed choice can be made between whole-blood tests and $^{13}$C-urea–based tests for applying the "test and eradicate" strategy in the office.

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